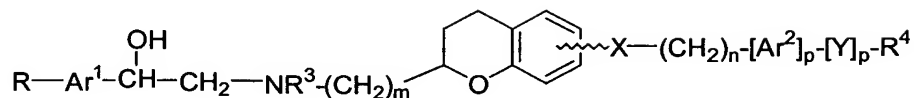


What is claimed as new and useful is:

1. A compound of the formula I:



5

I

wherein

R is hydrogen, hydroxy, oxo, halo, C₁-C₁₀haloalkyl, C₁-C₁₀ alkyl, cyano, nitro, NR¹R¹,
S R¹, OR¹, SO₂R², OCOR², NR¹COR², COR², NR¹SO₂R²,

10

NR¹CO₂R¹, pyrrole, or Ar², optionally substituted with hydroxy, halogen,
cyano, NR¹R¹, SR¹, trifluoromethyl, OR¹, C₃-C₈ cycloalkyl, phenyl,
NR¹COR², COR², SO₂R², OCOR², NR¹SO₂R², or NR¹CO₂R¹;

R¹ is hydrogen, C₁-C₁₀ alkyl optionally substituted with 1 to 4 substituents

15

selected from hydroxy, halogen, CO₂H, CO₂C₁-C₁₀ alkyl, SO₂C₁-C₁₀alkyl,
C₁-C₁₀ alkoxy; or C₃-C₈ cycloalkyl, phenyl or naphthyl, each optionally
substituted with 1 to 4 substituents selected from halogen, nitro, oxo, C₁- C₁₀
alkyl, C₁-C₁₀ alkoxy, and C₁-C₁₀ alkylthio;

R² is R¹ or NR¹R¹;

R³ is hydrogen, C₁-C₁₀ alkyl or $R-Ar^1-\overset{\text{HO}}{\underset{|}{CH}}-CH_2-$;

Ar¹ is Ar¹-O-CH₂, phenyl, or a 5 or 6 membered heterocyclic ring with from 1 to 4

20

heteroatoms selected from O, S and N, each moiety being optionally fused to
a 5 membered heterocyclic ring containing from 1 to 4 hetero atoms selected
from O, S, and N, the fused heterocyclic ring being optionally fused to a phenyl
ring or substituted with oxo;

m is 1, 2 or 3;

25

(CH₂)_m may be optionally replaced with C-O-(CH₂)_m;

X is SO₂-piperiziny, NR³--SO₂, or SO₂—NR³;

n is 0, 1, 2, 3, or 4;

Ar² is phenyl, or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S and N, each moiety being optionally substituted with halogen, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, and OR, or being fused to a 5 membered heterocyclic ring containing from 1 to 4 hetero atoms selected from O, S, and N, the fused heterocyclic ring being optionally fused to a phenyl ring or optionally substituted with oxo;

Y is O - Y, NR¹, NR¹CO, C₃-C₈ cycloalkyl or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S and N, each of which is optionally substituted with oxo;

p is 0 or 1;

R⁴ is hydrogen, R¹, R², oxo, C₁-C₁₀ heteroalkyl, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl, each being optionally substituted with C₃-C₈ cycloalkyl, phenyl, naphthyl, benzofuran, carbazole, dibenzothiofuran, or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S, and N, each ring structure being optionally substituted with halo and C₁-C₁₀ alkyl,

and pharmaceutically acceptable salts and esters thereof.

2. A compound of claim 1 wherein Ar¹ is optionally substituted phenyl or pyridyl, X is NR³-SO₂ or SO₂-NR³, Ar² is phenyl, pyridyl, pyrimidinyl or pyrrolyl, Y is optionally substituted pyridyl, pyrrolyl, pyrimidinyl, quinolinyl, imadazolyl, and dihydrobenzofuranyl, and R⁴ is R¹ or optionally substituted C₁-C₁₀ alkyl.

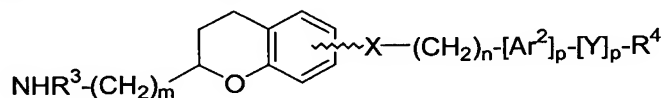
3. A compound of claim 2 wherein m is one and n is zero or one.

4. A compound of Claim 3 wherein R³ is hydrogen and R⁴ is C₁-C₁₀ alkyl optionally substituted with optionally substituted C₃-C₈ cycloalkyl, phenyl, or pyridyl.

5. A compound of claim 4 wherein R is hydrogen, halo, C₁-C₁₀ alkyl, nitro or NR¹R¹, n is zero, X is attached to the chroman moiety in the 6 position, n is zero, Ar² is phenyl or pyridyl, and Y is optionally substituted pyridyl or pyrrolyl.

6. A compound of Claim 1 wherein the -OH group of the compound of Formula 1 is in the R configuration.

7. A compound useful in the preparation of compounds of Formula 1 of the formula



Formula II/Compound 2

wherein,

R is hydrogen, hydroxy, oxo, halo, C₁-C₁₀haloalkyl, C₁-C₁₀ alkyl, cyano, nitro, NR¹R¹,
S R¹, OR¹, SO₂R², OCOR², NR¹COR², COR², NR¹SO₂R²,

NR¹CO₂R¹, pyrrole, or Ar², optionally substituted with hydroxy, halogen,
cyano, NR¹R¹, SR¹, trifluoromethyl, OR¹, C₃-C₈ cycloalkyl, phenyl,
NR¹COR², COR², SO₂R², OCOR², NR¹SO₂R², or NR¹CO₂R¹;

R¹ is hydrogen, C₁-C₁₀ alkyl optionally substituted with 1 to 4 substituents

selected from hydroxy, halogen, CO₂H, CO₂C₁-C₁₀ alkyl, SO₂C₁-C₁₀alkyl,
C₁-C₁₀ alkoxy; or C₃-C₈ cycloalkyl, phenyl or naphthyl, each optionally
substituted with 1 to 4 substituents selected from halogen, nitro, oxo, C₁- C₁₀
alkyl, C₁-C₁₀ alkoxy, and C₁-C₁₀ alkylthio;

R² is R¹ or NR¹R¹;

R³ is hydrogen, C₁-C₁₀ alkyl or
$$\text{R}-\text{Ar}^1-\overset{\text{HO}}{\underset{|}{\text{CH}}}-\text{CH}_2-$$
;

m is 1, 2 or 3;

(CH₂)_m may be optionally replaced with C-O-(CH₂)_m;

X is SO₂-piperiziny, NR³--SO₂, or SO₂—NR³;

n is 0, 1, 2, 3, or 4;

Ar² is phenyl, or a 5 or 6 membered heterocyclic ring with from 1 to 4

heteroatoms selected from O, S and N, each moiety being optionally

substituted with halogen, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, and OR, or being fused to
a 5 membered heterocyclic ring containing from 1 to 4 hetero atoms selected
from O, S, and N, the fused heterocyclic ring being optionally used to a phenyl
ring or optionally substituted with oxo;

Y is O - Y, NR¹, NR¹CO, C₃-C₈ cycloalkyl or a 5 or 6 membered heterocyclic ring
with from 1 to 4 heteroatoms selected from O, S and N, each of which is
optionally substituted with oxo;

p is 0 or 1;

R⁴ is hydrogen, R¹, R², oxo, C₁-C₁₀ heteroalkyl, C₁-C₁₀ alkyl, C₁-C₁₀ haloalkyl,
each being optionally substituted with C₃-C₈ cycloalkyl, phenyl, naphthyl,

benzofuran, carbazole, dibenzothiofuran, or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S, and N, each ring structure being optionally substituted with halo and C₁-C₁₀ alkyl,

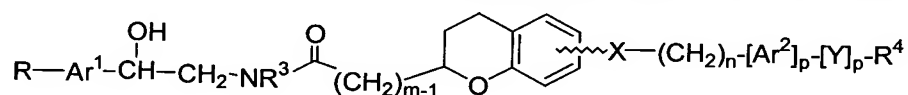
8. A compound of claim 7 wherein X is NR³-SO₂ or SO₂-NR³, Ar² is phenyl, pyridyl, pyrimidinyl or pyrrolyl, Y is optionally substituted pyridyl, pyrrolyl, pyrimidinyl, quinolinyl, imadazolyl, and dihydrobenzofuranyl, and R⁴ is R¹ or optionally substituted C₁-C₁₀ alkyl.

9. A compound of claim 8 wherein m is one and n is zero or one.

10. A compound of Claim 9 wherein R³ is hydrogen and R⁴ is C₁-C₁₀ alkyl optionally substituted with optionally substituted C₃-C₈ cycloalkyl, phenyl, or pyridyl.

11. A compound of claim 10 wherein n is zero, X is attached to the chroman moiety in the 6 position, n is zero, Ar² is phenyl or pyridyl, and Y is optionally substituted pyridyl or pyrrolyl.

12. A compound useful in the preparation of compounds of Formula 1 of the formula



Formula III/Compound 34

wherein

R is hydrogen, hydroxy, oxo, halo, C₁-C₁₀haloalkyl, C₁-C₁₀ alkyl, cyano, nitro, NR¹R¹, SR¹, OR¹, SO₂R², OCOR², NR¹COR², COR², NR¹SO₂R²,

NR¹CO₂R¹, pyrrole, or Ar², optionally substituted with hydroxy, halogen, cyano, NR¹R¹, SR¹, trifluoromethyl, OR¹, C₃-C₈ cycloalkyl, phenyl, NR¹COR², COR², SO₂R², OCOR², NR¹SO₂R², or NR¹CO₂R¹;

R¹ is hydrogen, C₁-C₁₀ alkyl optionally substituted with 1 to 4 substituents

selected from hydroxy, halogen, CO₂H, CO₂C₁-C₁₀ alkyl, SO₂C₁-C₁₀alkyl, C₁-C₁₀ alkoxy; or C₃-C₈ cycloalkyl, phenyl or naphthyl, each optionally substituted with 1 to 4 substituents selected from halogen, nitro, oxo, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, and C₁-C₁₀ alkylthio;

R² is R¹ or NR¹R¹;

R³ is hydrogen, C₁-C₁₀ alkyl or $\overset{\text{HO}}{\underset{|}{R-Ar^1-CH-CH_2-}}$;

Ar¹ is Ar¹-O-CH₂, phenyl, or a 5 or 6 membered heterocyclic ring with from 1 to 4

heteroatoms selected from O, S and N, each moiety being optionally fused to a 5 membered heterocyclic ring containing from 1 to 4 hetero atoms selected from O, S, and N, the fused heterocyclic ring being optionally fused to a phenyl ring or substituted with oxo;

5 m is 1, 2 or 3;

$(CH_2)_m$ may be optionally replaced with $C-O-(CH_2)_m$;

X is SO_2 -piperizinyl, NR^3-SO_2 , or SO_2-NR^3 ;

n is 0, 1, 2, 3, or 4;

10 Ar^2 is phenyl, or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S and N, each moiety being optionally substituted with halogen, C_1 - C_{10} alkyl, C_1 - C_{10} alkoxy, and OR, or being fused to a 5 membered heterocyclic ring containing from 1 to 4 hetero atoms selected from O, S, and N, the fused heterocyclic ring being optionally fused to a phenyl ring or optionally substituted with oxo;

15 Y is O - Y, NR^1 , NR^1CO , C_3 - C_8 cycloalkyl or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S and N, each of which is optionally substituted with oxo;

p is 0 or 1;

20 R^4 is hydrogen, R^1 , R^2 , oxo, C_1 - C_{10} heteroalkyl, C_1 - C_{10} alkyl, C_1 - C_{10} haloalkyl, each being optionally substituted with C_3 - C_8 cycloalkyl, phenyl, naphthyl, benzofuran, carbazole, dibenzothiofuran, or a 5 or 6 membered heterocyclic ring with from 1 to 4 heteroatoms selected from O, S, and N, each ring structure being optionally substituted with halo and C_1 - C_{10} alkyl.

25 13. A compound of claim 12 wherein Ar^1 is optionally substituted phenyl or pyridyl, X is NR^3-SO_2 or SO_2-NR^3 , Ar^2 is phenyl, pyridyl pyrimidinyl or pyrrolyl, Y is optionally substituted pyridyl, pyrrolyl, pyrimidinyl, quinolinyl, imadazolyl, and dihydrobenzofuranyl, and R^4 is R^1 or optionally substituted C_1 - C_{10} alkyl.

14. A compound of claim 13 wherein m is one and n is zero or one.

30 15. A compound of Claim 14 wherein R^3 is hydrogen and R^4 is C_1 - C_{10} alkyl optionally substituted with optionally substituted C_3 - C_8 cycloalkyl, phenyl, or pyridyl.

16. A compound of claim 15 wherein R is hydrogen, halo, C_1 - C_{10} alkyl, nitro or NR^1R^1 , n is zero, X is attached to the chroman moiety in the 6 position, n is zero, Ar^2 is phenyl or

pyridyl, and Y is optionally substituted pyridyl or pyrrolyl.

17. A method of treating a beta-3 adrenergic receptor mediated condition which comprises administering to a patient in need thereof a pharmaceutically effective amount of a compound of Formula 1, or a salt or ester thereof.

5 18. A method of treating a beta-3 adrenergic receptor mediated condition which comprises administering to a patient in need thereof a pharmaceutically effective amount of a compound of claim 9, or a salt or ester thereof.

10 19. A method of treating obesity in mammals which comprises administering to a patient in need thereof a pharmaceutically effective amount of a compound of Formula 1, or a salt or ester thereof.

20. A method of treating obesity in mammals which comprises administering to a patient in need thereof a pharmaceutically effective amount of a compound of claim 9, or a salt or ester thereof.

15 21. A method of treating diabetes in mammals which comprises administering to a patient in need thereof a pharmaceutically effective amount of a compound of Formula 1, or a salt or ester thereof.

22. A method of treating diabetes in mammals which comprises administering to a patient in need thereof a pharmaceutically effective amount of a compound of claim 9, or a salt or ester thereof.

20 23. A pharmaceutical composition comprising an effective amount of a compound of Formula I or a pharmaceutically acceptable salt thereof in combination with a pharmaceutically acceptable carrier.

24. A composition comprising an effective amount of a compound of Formula I, or a salt hereof, in combination with an inert carrier.